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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,453	01/03/2001	Samario Chaitchik	381/25	2182

7590 09/13/2002

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EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	8

DATE MAILED: 09/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/752,453	Applicant(s) CHAITCHIK ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 6/4/02 in Paper No. 7 is acknowledged and has been entered. Claim 1 has been amended. Currently, claims 1-13 are pending and are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 remains incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Specifically, the preamble is drawn to a method that requires testing of drug sensitivity of cells; however, a correlation step of how it is determined that cells are sensitive to the drug, has not been recited. In step e) the recitation of "correlating a result of an assay ... to the drug sensitivity", does not appear to meet the requirement of the preamble.

Claim 1, step b) is ambiguous in reciting, "exposing a portion of the cells to a drug" because the term "a portion" is a relative term that lacks a comparative basis for defining its metes and bounds. Specifically, how is the portion of cells selectively

exposed to a portion, i.e. a subset, of the cells; does this step involve a ligand that specifically binds specific cell subsets. Please clarify.

Claim 1, step e) is confusing in lacking structural and functional cooperative relationships between the assay device, the cells in defined locations in the instant step, and the drug and the substance capable of producing fluorescence in steps b) and c), respectively. For example, does the drug cause intracellular activity in the cells that render them sensitive, does the substance capable of imparting fluorescence fluoresce selectively only when intracellular activity in the sensitive cells is present or is there an increase or decrease in the fluorescence, how is the result from sensitive cells distinct and different from cells that do not manifest sensitivity to the drug. Step e) merely recites that an assay is performed by means of an assay device to obtain a result and to determine and correlate the result with drug sensitivity, but fails to provide exactly how the test is performed, in addition to adding the drug and the label to the supposed subset of cells that are caused to reside in defined locations.

Claim 10 is indefinite in reciting, " further including the step of" because it is unclear what other steps that are not recited are "further included" in the claim. Perhaps, Applicant intends use of the term "further comprising" so as to be consistent with claim 1 from which it depends.

Claim 11 is indefinite in reciting, " further including the step of" because it is unclear what other steps that are not recited are "further included" in the claim. Perhaps, Applicant intends use of the term "further comprising" so as to be consistent with claims 1and 11, from which it depends.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide any literal support for the recitation of "wherein the drug and said substance capable of imparting a measurable degree of fluorescence are separately applied". Applicant points to Examples 1 and 2 for support which discloses that 1) that the cells are dyed or stained with Rh123, FDA, or AO and 2) that Navelbine and 5-Fluorouracil (5FU) are added to the cells at low doses and high doses to T80 and T47D cells for 24 hours, 48 hours, and 72 hours but fails to provide any literal support for such recitation, or support limiting distinctly and descriptively, such a recitation. Furthermore, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal and distinct descriptive support in the specification or originally filed claims constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,180,343) in view of (Weinreb et al. (US 4,729,949).

Anderson et al. disclose a method of testing sensitivity of cells to drugs comprising candidate nucleic acids. Anderson et al. teach preparing a suspension of cells then exposing the cells to the nucleic acids. Nucleic acids are encapsulated with liposome then are introduced into the cells by liposome fusion. The cells are incubated and cultured to optimize growth and proliferation of the cells, then are timely harvested. See column 19, line 38 bridging to column 20, line 3. Exogenous nucleic acids are also introduced by viral infection (see column 20, lines 45-54). The drug sensitivity method allows selection of cells that exhibit sensitivity by virtue of altered phenotype as a consequence of the presence of the peptide within the cell (see column 20, line 64 to column 21, line 16). Anderson et al. also teach labeling the nucleic acid with GFP or fluorescent dyes to impart a measurable degree of fluorescence (see column 22, lines 32-41). Cells exhibiting an altered phenotype or change in physiology is due to the sensitivity of the cells to the nucleic acid as a bioactive peptide. These phenotypic alterations or pharmacologic effects are manifested depending on the sensitivity of cells to the nucleic acid (see columns 23-24 and 35). Accordingly, sensitivity of cells to the nucleic acid is detected and measured by microscopic analysis of cellular morphology,

standard assay for the presence of a particular cell or molecule manifested by the phenotypic alteration, and flow activated cell sorting (FACS) (see column 23, lines 54-67). Anderson et al. teach detecting and measuring GFP using scanning densitometer, BioImage software, and BD FACSCAN and calculating specific fluorescence, i.e. ratio of the average fluorescence to the relative intensity and standard deviation of fluorescence intensity (see column 38).

Anderson et al. differ in failing to disclose causing the cells to reside individually in defined locations wherein each individual cell corresponds to the defined location and accessed individually by an assay device for assaying and determining the sensitivity of the drug.

Weinreb et al. disclose a method for placing individual living cells at defined locations wherein a fluid containing living cells is applied to a carrier having a plurality of apertures arranged in an ordered array and sized specifically to hold individual cells. The cells are cause to migrate into the apertures to the defined locations by applying a force or pressure differential (see Abstract and column 8, line 58 to column 9, line 13). Excessive and other cells are washed off at least once. The fluorescence of each cell on the defined locations in the carrier is separately measured and recorded. Examples of measurable and calculable parameters include fluorescence intensity, degree of fluorescence polarization, light scatter, optical density, electromagnetic properties, and information or data obtained is processed, recorded, plotted, and stored in a computer system. Standard errors are obtained by comparison to control values for recordation to

eliminate outliers from values within a standard deviation (see columns 16-18 and 23-24).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have harvested the cells in the method of Anderson for drug sensitivity assaying using the cell carrier system taught by Weinreb because Weinreb specifically taught that the carrier provides better separation of cells that have been selected for assaying; thus enabling better determination and accuracy in testing for drug sensitivity of cells selected.

5. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,180,343) in view of (Weinreb et al. (US 4,729,949) as applied to claims 1-4 and 7-13 above, and further in view of Condon et al. (US 6,168,944).

Anderson et al. and Weinreb et al. have been discussed supra. Anderson et al. and Weinreb et al. differ in failing to disclose harvesting the cells using trypsin.

Condon et al. teach large scale cultivation cells wherein trypsin is used to dissociate and harvest cells from microcarriers in bioreactors.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have harvested the cells in the method of Anderson as modified by Weinreb using trypsin to dissociate the cells from microcarriers because Condon specifically taught that trypsin is a known proteolytic enzyme for use in dissociating and harvesting cells in large scale cultivation of cells such as in the methods disclosed by Anderson and Weinreb.

Response to Arguments

6. Applicant's arguments filed 5/31/02 have been fully considered but they are not persuasive.

A) Applicant argues that claim 1, as amended, recites that the drug and the substance capable of imparting a measurable degree of fluorescence, is separately applied, and that Anderson does not teach such a limitation since Anderson teaches introducing a molecular library of fusion nucleic acids encoding randomized peptides fused to GFP into a plurality of cells.

In response, such limitation fails to be literally or distinctly supported by the specification. Additionally, contrary to Applicant's argument, Andersen, indeed, discloses that other labels including fluorescent dyes and isotopes are attached or added, i.e. separately applied, and not necessarily in fusion, with the candidate nucleic acid.

Additionally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to separately apply the drug and the fluorescent label upon the cells to test for drug sensitivity because it has been held that constructing what would have been an integral structure in various separate elements, i.e. for separate application, involves only routine skill in the art. *Nerwin v. Erlichman, 168 USPQ 177,179.*

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
September 9, 2002

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641